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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/681,418	10/07/2003	H. Michael Shepard	NB 2008.01 (060925-0801)	7416

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EXAMINER	
CRANE, LAWRENCE E	
ART UNIT	PAPER NUMBER
1623	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/681,418	SHEPARD ET AL.	
	Examiner	Art Unit	
	L. E. Crane	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *July 24, 2006 (amdt)*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *53-57,59-61,63,64,68-70,79,80 and 83-93* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *53-57,59-61,63,64,68-70,79,80 and 83-93* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/16/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims **58, 62, 73-76 and 78** have been cancelled, claims **53-57, 63, 68, 83-84, 88-90 and 92-93** have been amended, the disclosure has been amended, and no new claims have been added as per the amendment filed July 24, 2006. No additional or supplemental Information Disclosure Statements (IDSs) have been filed as of the date of this Office action.

Claims **53-57, 59-61, 63-64, 68-70, 79-80 and 83-93** remain in the case.

Claims **60, 63-64, 68-70, 79-80 and 83-93** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one of ordinary skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The fundamental issue here is whether practicing the full scope of the instant invention is possible without undue experimentation. As provided for in *In re Wands* (858 F.2d 731, 737; 8 USPQ 2d 1400, 1404 (Fed Cir. 1988) the minimum factors to be considered in determination of whether a conclusion of "undue experimentation" is appropriate are as follows:

A. The breadth of the claims extends to isomeric compounds the synthesis of which has not been defined in a manner permitting one of ordinary skill to know the identity of the compounds which have shown activity in the treatment of neoplastic disease conditions. In addition, claim **63** identifies compounds the synthesis and biological testing of which has not been disclosed, including
i) "wherein the compound may be in any enantiomeric, diastereoisomeric or stereoisomeric form, including ... L-form, α-anomeric form." Only D-forms are disclosed as having been synthesized and as having the desired medicinal activity, and
ii) because there is no showing of either how to make or use the compounds defined by claims **83 and 84**.
In addition, applicant has not supplied any data to support the extension of treatments to include "liver cancer."

B. The nature of the invention is directed to 5-substituted-2'-deoxyuridines and analogues thereof as defined by claim **63**, pharmaceutical compositions thereof, a method of testing for relative antineoplastic activity, and method of treating several different neoplastic disease conditions.

C. The state of the prior art is well established by the extensive lists of prior art patents and other references disclosed by the patents issued to Shepard and Shepard et al. listed on the instant PTO-892.

D. The level of one or ordinary skill is high because the practice of the invention requires knowledge of both the organic synthesis of nucleoside analogues and the medical knowledge and training required to properly administer and monitor antineoplastic agents to a host in need thereof.

E. The level of predictability in the art is limited because the number of compounds actually synthesized and/or tested, and the specific disease conditions tested, is very small when compared with the number of compounds included within the scope of the instant claims. In view of the lack complete test data, it is also unclear that the substitution of "Cl," or "I" for "Br" as an X-substituent will produce equivalent biological testing results. Similarly, most of the variations provided for by the alternatives within the definitions of variables R^6 and R^7 have neither been synthesized nor tested for biological activity. And, only three neoplastic cell types have been shown to be effectively inhibited. For this reason examiner concludes that the asserted and claimed extrapolation to the effective treatment of all "pathological" cell types which overexpress thymidylate synthase is not sufficiently predictable and therefore not adequately enabled.

F. The amount of direction provided by the inventor is difficult to determine because of incomplete synthetic information and incomplete identifying information concerning the identity of compounds tested for biological activity at pages 68-69. Applicant has not provided enabling support for the synthesis of "any enantiomeric, diastereomeric or stereoisomeric form," and in particular has not shown how to make the L-forms and the α-anomers of any of the claimed compounds, or shown that the asserted and claimed pharmaceutical activity or testing for said activity of claims **87-93** extends to all possible enantiomers and diastereomers and other than ß-D-isomers of some of the compounds defined by claim **63**.

G. The existence of working examples is difficult to determine because of incomplete identifying information concerning either the synthesis of many of the compounds claimed or the identity of compounds tested for biological activity at pages 68-69.

H. The quantity of experimentation needed to make or use the invention based on the content of the disclosure is deemed to be excessive in light of the very limited amount of biological test results and synthetic instructions provided for the compounds defined by claim **63**. In particular, the instant method of treatment claims are only enabled for the treatment of one variety of breast cancer, one variety of colon carcinoma, and one fibrosarcoma (HT 1080; organ apparently not specified in the disclosure) according to the table at page 70). There are no enabling examples for the claimed method of testing. Therefore, examiner concludes that the amount of experimentation required to practice all aspects of the instant claimed invention is undue in view of the lack of anything but prospective disclosure.

Applicant's arguments filed July 24, 2006 have been fully considered but they are not persuasive.

Examiner notes the narrowing of several claims definitions by deletion of functional language and has been amended both the claims listed and details of the above rejection in response thereto. Applicant has argued that the instant Example 16 is sufficient to show that the instant disclosure has enabled all manner of stereoisomers and how to make and use same. Examiner respectfully disagrees noting that 10 of the 12 compounds are 2'-deoxy-ß-D-uridine derivatives and that there are no L-ribofuranosyl analogues or other indicia of a breadth of substances having been made or tested to show that the extrapolations the instant claims relky on have been supported by actual results. See *Ex parte Balzarini et al.* 21, USPQ 2d 1892, 1894 (BPAI, 1991) standing in its first opinion stands for the proposition that claims directed to medicinal treatments of diseases in highly unpredictable art areas are properly rejected under 35 U.S.C. §112, first paragraph as lacking adequate enablement, in the absence of sufficient test data in support of the efficacy of the alleged treatment. For additional discussion of this decision, see MPEP at §2107.03.

Claims **54-56** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims **54-56** the term "E" and "Z" are nor properly applied because the 5'-substituent has two E/Z alternative opportunities. See Example 16 wherein compounds claimed herein are completely named. Examiner suggests either naming the compounds being claimed or making

specific which double bond geometry of the 5-substituent is being defined or other appropriate amendment to clarify the intended meaning.

Applicant's arguments with respect to claims **54-56** have been considered but are deemed to be moot in view of the new grounds of rejection. Applicant's amendment necessitated this new grounds of rejection.

The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel,* 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam,* 686 F. 2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi,* 759 F.2d 887, 225 USPQ 645 (Fed. Cir 1985); and *In re Goodman,* 29 USPQ 2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. §1.78(d).

Effective January 1, 1994, a registered attorney or agent or record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R. §3.73(b).

Claims **53-57, 59-61, 63-64, 69-70, 79-86 and 91-93** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1-10*** of U.S. Patent No. **6,683,061** (PTO-892 ref. **AB**). Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of treatment and the alleged active ingredients are directed to substantially overlapping subject matter.

Applicant's arguments filed July 24, 2006 have been fully considered but they are not deemed to be persuasive.

Applicant's arguments filed November 29, 2005 have deferred responding to the instant grounds of rejection pending a finding of allowable subject matter. No further comment on

this rejection has been included within the instant response. Therefore, the instant rejection has been maintained.

Claims **87-90** would be allowable if rewritten or amended to overcome the rejection under 35 U.S.C. §112.

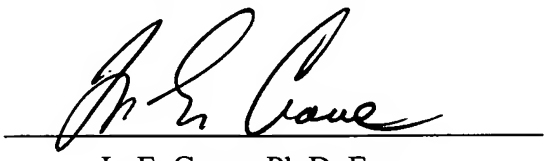
Papers related to this application may be submitted to Group 1600 via facsimile transmission(FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX directly to Examiner's computer is 571-273-0651. Telephone number for filing documents officially by FAX with the USPTO is **571-273-8300**.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. S. Anna Jiang, can be reached at **571-272-0627**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

LECrane:lec
03/31/2007



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